

THROMBOCYTOPENIA INDUCED BY VINOURELBINE, DOXORUBICIN AND CISPLATIN IN HUMAN CANCER PATIENTS

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SUMMARY

Cancer is fatal dilemma of human life. During the recently ended 20th century, it was the more feared and in many ways, the most mysterious of the major life threatening diseases of the world. Despite of surprising advancement in applied therapeutics, cancer is still, both in perception and reality, a very real concern of public health. Therefore present retrospective study was aimed to investigate the thrombocytopenia in cancer patients. A total of 60 adult cancer patients selected with non-small cell lung cancer (NSCL), metastatic breast cancer (MBC), and cancer of cervix, with age between 24 - 71 years (Mean 42.73, SEM±2.). They were divided in to two groups: Group-1 patients on the treatment protocol of Vinorelbine alone and group 2 patients on treatment protocol of Vinorelbine base combinations; Vinorelbine/ Doxorubicin and Vinorelbine/ Cisplatin. The results obtained were statically analyzed. On comparison of overall mean values over time, the insignificant thrombocytopenia observed in the patients on chemotherapy protocol of Vinorelbine alone and Vinorelbine based combination. By an independent comparison of mean values of two group at every week, a significantly thrombocytopenia seen at week 1 in the patients on treatment protocol vinorelbine based combinations. When the mean value observed before therapy compared with that of at week-4 of both of the groups, there was insignificant decrease noted in thrombocyte count. This study has pointed out insignificant differences in the overall thrombocytopenic syndrome observe in both of the chemotherapy protocols. The clinical pharmacist, medical oncologist, and consultant physician, may therefore suggested to select either of the chemotherapy protocol. The therapeutical efficacy is more important while constituting the overall management of a particular neoplasm.

Keywords: Thrombocytopenia, Vinorelbine, Cisplatin, Doxorubicin, Breast Cancer, NSCL Cancer

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INTRODUCTION

Surprising advancement in applied therapeutics does not assure absolute treatment of neoplasm. Cancer is still a very real concern of public health. It is being treated stereoscopically with good or bad results by using surgical, radiological or chemotherapeutic methods (1). Restoring of tumor suppresser gene P53 might suppress tumor growth and cause “programmed cell death” of cancer cell (2). Present therefore aimed to investigate the thrombocytopenia in cancer patients.

Chemotherapeutical agents are used extensively in cancer treatment. Which, besides producing cure, exert deleterious effects on the body metabolism and bring structural and physiological changes in vital organs of the body.

These drugs can damage the blood producing cells of bone marrow and patient may have low blood count resulting in bleeding after minor cuts or injuries (due to shortage of platelets), increased chance of infection (leukopenia) and fatigue or shortage of breath (due to lower RBCs count) (3).

There are several types and stages of chemotherapy used to treat cancer i.e. induction therapy, consolidation therapy, intensification therapy, maintenance therapy, adjuvant therapy, palliative therapy, and chemo-preventive therapy (16).

In this study, the thrombocytopenia induced by Vinorelbine alone and Vinorelbine based combinations (Vinorelbine/ Doxorubicin and Vinorelbine and Cisplatin) were studies to evaluate their therapeutical credibility. The platelet count, pre & post chemotherapy was also calculated to assess the comparative thrombocytopenia.

MATERIALS AND METHODS

This retrospective research study was conducted to investigate thrombocytopenia of adult cancer patients with Non small cell lung cancer, metastatic breast cancer, and of cervix, being treated with Vinorelbine and Vinorelbine based combinations.

Study parameter

The cancer diagnosed patients, on treatment protocol of vinorelbine as part of their chemotherapy were investigated for alterations in platelets count (thrombocytopenia).

Study Design

A total 60 cancer patients irrespective of their age, sex, status and occupation selected from out patient department (OPD), and wards of hospitals. These patients were then divided into two groups. Group-1 comprised of forty five (45) cancer patients taking vinorelbine as single therapy and Group-2 comprised of fifteen (15) cancer patients but on treatment protocol of vinorelbine based combinations i.e. Vinorelbine/Cisplatin vinorelbine/Doxorubicin. The clinical tests for alterations in platelets count were performed by an automatic computerized Auto-analyzer in the Pathology Laboratory of hospital. The blood samples were drawn from brachial veins; 3 ml of blood was taken in 5c.c disposal syringe and then pushed in to C.B.C (complete blood count) vial, containing 20wro EDTA anti-coagulant. This vial was distinguished from other sample vials by its lavender top colored cap.

Chemical and Reagents

The materials, chemicals and instruments used comprised of 5 ml disposable syringes; complete blood count (CBCs) vial, normal saline (0.9% sodium chloride), $\frac{1}{2}$ normal saline (0.45% sodium chloride), 5% dextrose (glucose) in sterile water, non-pyrogenic IV infusion (Otsuka), anticancer drugs –Vinorelbine (Navelbine): 10mg/ml and 50mg/5ml injection solution in vial, manufactured by Pierre Fabre Oncologic Laboratories, France, Doxorubicin hydrochloride USP (Deldoxin): 2mg/ml injection solution manufactured by Pharmacia & Upjohn (Perth) limited, Bently, Australia. Cisplatin (Cisplatinum): vials of 10mg/20ml, 25mg/50ml and 50mg/100ml Cisplatin Laboratories, Austria, Auto-analyzer (or CBC-Analyzer) Technicon 113, of Byer Laboratories USA.

Preparations of Standard Regimen of Chemotherapeutical Agents

Vinorelbine a mitotic spindle poison (antineoplastic) is available as 10mg/ml or Vinorelbine 50mg/ml. The Navelbine 10mg/ml injection solution in vial contains Vinorelbine ditartate 13.85mg quantity corresponding to Vinorelbine (base) 10.00 mg with water for injection sufficient quantity to make one full vial and Navelbine 50 mg/5ml injection solution in vial contain Vinorelbine ditartate 69.25mg quantity corresponding to Vinorelbine (base) 50.00 mg with water for injection sufficient quantity to make one full vial (4). The dose and protocol of Vinorelbine was as to administer 25 mg/m² on day 1, weekly 4, i/v, with 0.45% sodium chloride or 5% glucose solution as diluents and delivered over IVP (15). The injected dose was diluted in normal saline solution (i.e. 125 ml) and infused over a short period -15 to 20 minutes (5). The administration was followed by a vein wash out using isotonic solution (6). In combination chemotherapy, the dose and frequency of administration was decided taking in to account stage and morphology of the neoplasm patient's condition and respective dose and protocol regimes (6).

In combination form the dose of Vinorelbine was as to administer 20 mg/m² on day 1, 8 I/V with diluent day 5 $\frac{1}{2}$ NS and delivered over intra venous push (IVP). The Doxorubicin was given as 50 mg/m² on day 1 only as I/V with diluent 0.9% Sodium Chloride or 5% Glucose solution (repeated Q 3 weeks) (7). The dose schedule was 50mg/m² body surface area, given as single intravenous injection at 21st day interval (6) Doxorubicin was administered slowly in to tubing of freely running infusion of Sodium Chloride 0.9% or Glucose 5%. (8).

The Cisplatin is platinum derivative cytotoxic drug (6) and is available as 2ml vial containing 1mg Cisplatin as active ingredient. It is administered intra-venously as 40mg/m² on day 1 only with the diluent of day 5 $\frac{1}{2}$ NS and delivered over IVP. The Cisplatin administered intravenously with 500 c.c. normal saline diluent at the dose rate for adults and children 40mg/m² on day 1 of chemotherapy course. It was delivered over 2 hours. The Vinorelbine was administered as 20mg/m² on day 1, 8 , I/V with Diluent day 5 $\frac{1}{2}$ NS and delivered over IVP (intravenous push) For breast cancer the Vinorelbine single therapy (5) and Vinorelbine / Doxorubicin combination therapy (9) where applied???, for combination therapy (10) where used vial?? for cervix cancer the Vinorelbine /Cisplatin treatment was given to the patients. There was a criteria established to approach the patients having required characteristics i.e. the patients with definitive diagnosis of cancer, patients had not previous history of a severe systemic disease, especially relating to the hemic system, the patient with normal base line blood profile.

Laboratory analysis

The blood samples were drawn from brachial vein. 3ml of the blood was collected in 5cc disposable syringe and then pushed into CBC vial, containing 20ul EDTA anticoagulant. This vial was distinguished from other sample by lavender top colored cap. This autoanalyzer made to suck the sample manually and the results were displayed on screen. The autoanalyzer validated and standardized before using to perform the tests.

Data Interpretation and Analysis

The data collected is manipulated and analyzed statistically to explore some clinically important findings.

RESULT AND DISCUSSION:

The P values of mean platelet counts of cancer patients on treatment protocol of Vinorelbine (Group-I) was obtained as 0.423 (103) per uL, Vinorelbine based combination (Group-II) 0.431 (103) per uL and overall (60) patients 0.380 (103) per uL. By the overall comparison of mean values overtime, there was insignificant thrombocytopenia observed in the patient on both of the two groups.

The obtained P values of mean SEM \pm Platelets count (103) per uL of two groups at every week pre and post chemotherapy of cancer patients of Group-I, Group-II and overall total (60) patients were 0.270 at W0, 0.004 at W1, 0.111 at W2, 0.131 at W3 and 0.135 at W4. By an independent comparison of mean values of two groups at every week, there was significant thrombocytopenia observed at week 1 only, in the patients of G-II.

The obtained P values of mean SEM \pm Platelets count (103) per uL observed before therapy with that of at week-4, pre and post chemotherapy of cancer patients of Group-I was 0.949 and Group-II 0.297. When the mean values observed before therapy was compared with that of week- 4, an insignificant thrombocytopenia noted in patients of G-I and G-II.

Shamseddine et al, (17), have been reported an acceptable thrombocytopenia induced by Cisplatin/Vinorelbine combination. Krajnik, et al (18) have further shown the dose limiting thrombocytopenia produced by Vinorelbine and Gemcitabine in NSCL cancer. Mrty, et al (14) have been reported thrombocytopenia except in pretreated ovarian cancer patients. Henry & Tretton, et al., (11), Gasparini, et al., (12), Fumoleau, et al., (13) have further speculated insignificant thrombocytopenia in the cancer patients treated with the Vinorelbine as alone and combination with other cytotoxic drugs.

Thus in conclusion, the reported results have validated the insignificant difference in the overall thrombocytopenic syndrome induced by both of the chemotherapy protocols. The clinical oncologist, consultant physician and pharmacist, therefore can probably select either of the protocol. The efficacy should probably constitute the treatment of NSCL, breast and cervix cancer.

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